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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,482	08/23/2001	Naoya Motegi	ASA-1025	8422

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EXAMINER	
SODERQUIST, ARLEN	
ART UNIT	**PAPER NUMBER**
1743	

DATE MAILED: 02/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/934,482	MOTEGI ET AL.	
	Examiner	Art Unit	
	Arlen Soderquist	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 August 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9-23-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the means for washing at least the reagent probe must be shown or the feature(s) canceled from the claim(s). It is noted that there is only a general description of the washing structure. No new matter should be entered.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

2. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear what type of cross-contamination is being detected: a first reagent in a sample that is being measured using a second reagent, contamination of a first reagent in its container with a second reagent or contamination (reagent or reaction byproducts) left behind in a sample cup due to incomplete cleaning of the sample cup. It is also not clear if there is a relationship between the cross-contamination and the newly added language directed toward the pipetting mechanism. For examination purposes the claim is being treated as broad enough to cover all of the possible sources of contamination listed above and no connection between the pipetting mechanism and the contamination is being required. If it is measurements of actual samples that go into the contamination judgment process of the independent claims, it is also not clear what the measurement process is to make the judgment on the presence or absence of cross-contamination. Does the measurement process include multiple measurements of the same

sample that are compared or are results from different samples that are compared to make the contamination judgment? It is not clear if the function of claims 4 and 9 are the same as or different from the function to set determination conditions for judging the presence or absence of cross contamination found in claims 1-2.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 1-4, 6, 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the admitted state of the art as defined by the Jepsen format of the original claims of the instant application or Sakagami (US 4,785,407) in view of Kopf-Sill (US 5,590,052) or Ginsberg (US 4,276,051).

The claim format used for the original claims is an improvement on an existing instrument and therefore being interpreted as the Jepsen format. In the first part of original claim 1, applicant admits an automatic chemical analyzer capable of determining plural components of a sample using independent (different) reagents for the respective components. At least a part or all of the sections for performing liquid transfer, mixing and determination of the reagents, samples and reaction solution under analysis are shared. In order to prevent the occurrence of errors of determination due to contamination, the analyzer is provided with a function to set the determination conditions for judging the presence or absence of contamination and to make an automatic judgment of the combination of items involving contamination. The admitted prior art does not teach how the judgment of contamination is made.

In the patent Sakagami teaches three embodiments of an automatic chemical analyzer including a cuvette wheel (1) having a number of cuvette holding recesses formed along a periphery thereof a driving unit (1A) for rotating the cuvette wheel in a stepwise manner, an automatic cuvette loader (3) for supplying cuvettes (2) into cuvette holding recesses of the cuvette wheel, a sample delivery device (4) for supplying samples into cuvettes held on the cuvette wheel, a reagent delivery device (5) for supplying a plurality of different reagents into cuvettes held on the cuvette wheel, at least one colorimeter (6-1,6-2,6-3) for measuring an optical density of test liquids contained in cuvettes, a washing device (7) for washing cuvettes, and an automatic cuvette unloader (8) for removing cuvettes out of the cuvette wheel. The analyzer further comprises a central control device for controlling the automatic cuvette loader and unloader such that after a cuvette has been repeatedly used a predetermined maximum number of times, the relevant cuvette is removed from the cuvette wheel and a new cuvette is supplied into the cuvette holding recess from which the cuvette has just been removed. Figure 2 shows the washing unit in detail. The second and third embodiments are shown in figures 4-7 and include a colorimeter (26) arranged in the washing unit to detect a degree of deterioration, stain or dirtiness (contamination/cross-contamination) of one or more cuvettes. An output signal of the colorimeter is supplied to the control device (24) and is compared with a tolerable threshold level which has been previously stored. When a detected level representing the dirtiness of a cuvette exceeds the threshold level, the relevant cuvette is discharged from the cuvette wheel even though the cuvette has not yet been used the maximum number of times. The invention may have many modifications including using the colorimeter as the sole determiner for when to exchange a cuvette, using a plurality of washing agent liquids that may be selectively supplied to a cuvette in accordance with a test item or using a detected concentration of substance contained in a sample as the condition for exchanging the cuvette when it is measured to be when an abnormally high. Column 2, lines 48-52 teaches that since the sample and reagent delivery devices are well known in the art, their detailed description is not given. Column 2, lines 62-65 teach that the reagent delivery device can deliver a specific reagent selected from a plurality of reagents. Sakagami does not teach using a difference between a previous measurement and a current measurement as the condition for determining the contaminated condition.

In the patent Kopf-Sill teaches error checking in a blood analyzer. The patent provides various methods for detecting errors in a blood analysis system. The system includes a blood analyzer and cuvettes that contain lyophilized reagents in a rotor. The rotor is placed in the analyzer, which spins the rotor, and an optical system reads the cuvettes as light is flashed through the cuvettes. There are checks for various things including things related to contamination: determining dilution systematic failure when measuring different reaction chemistries in the cuvettes of the rotor; determining whether a blood sample in a cuvette is hemolyzed, lipemic, or icteric; and determining the degradation of a reagent in a cuvette. Column 1, lines 58-65 teach it is desirable to provide methods for detecting these and other problems in order to avoid reporting of false results and improve the accuracy of the fluid analyzing process. The methods should be able to verify that individual readings and/or groups of readings fall within expected values and ranges and thus be able to produce an alarm when the readings are improbable and fall outside of the expected values and ranges. The paragraph bridging columns 3-4 teaches a method for determining if diluent in an analytical rotor has been contaminated by bacteria or other materials. In the method only diluent from a diluent source is distributed to a cuvette. Light is directed to the cuvette containing only diluent at a wavelength that is differentially absorbed by diluent having differing amounts of contamination and a resulting signal is measured. The signal measured is then compared with an expected value and an error is indicated if the measured signal differs by a predetermined amount from the expected value. A flow chart for this is shown in figure 6. In the comparison step, if the measured value differs from a diluent absorbance limit by a predetermined amount, an error is indicated that the diluent is contaminated and the rotor can be suppressed. In a preferred aspect, the measured signal is compared with the diluent absorbance limit to determine if the measured signal is greater than the limit. If so, an error signal is indicated. Figure 11 illustrates a method used to determine if a blood sample is contaminated: the blood sample is hemolyzed, lipemic, or icteric. This test is particularly useful for whole-blood analyzers where the user is not given a chance to visualize the serum or plasma and judge its hemolysis, lipemia, or icteric content. The method determines these levels by placing the blood in the rotor and spinning the rotor to deliver the plasma to the cuvettes. A cuvette having a sample blank reagent is then flashed with a series of light flashes having three different wavelengths, preferably, about 340, 405 and 467 nm. A

signal is measured for each of the three flashes and then compared in an iterative manner to determine whether the sample is hemolyzed, lipemic, or icteric. The calculations used in this comparison are referred to as sample index calculations. If one of these conditions is satisfied, an error condition is indicated. A further source of error can be in the handling of rotors after they leave the manufacturer's warehouse. Typically, the rotors are packaged in impermeable foil pouches with a desiccant pouch inside and shipped in cold packs to users who store them in cold storage, such as a refrigerator. Before use, the rotors are typically brought to room temperature for at least 20 minutes and generally no longer than 120 hours. Some of the chemistries are adversely affected by exposure to heat, humidity, light, and other environmental conditions resulting in contamination due to reagent degradation. To determine whether any of the reagents may have been affected by excessive exposure to such conditions, the method illustrated in figure 12 is used to generate an error condition if the rotor has been overexposed to heat, moisture, or to UV or other light. The check is performed by providing at least one test reagent in at least one cuvette that is more sensitive to heat, light, moisture, or other environmental conditions than all other analytical reagents in other cuvettes of the rotor. When the rotor is spun in the analyzer, only diluent is delivered to the cuvette having the test reagent(s). Light is then directed through the test cuvette and a signal is measured. If the signal differs by a predetermined amount from an expected value, the error condition is indicated.

In the patent Ginsberg teaches a system and program for progressively measuring the absorbance changes of a large number of aliquots from a plurality of different samples in a continuous processing mode. The device being substantially similar to that taught by Sakagami. A plurality of routine samples are maintained in an ordered sequence in a sample tray which may be moved to a first sample pick up position. Emergency samples (stats) and controls (standards) are positioned in a second plurality of auxiliary positions which may be moved to a second sample position. A first and second plurality of reagents are maintained, moved to respective reagent pick up positions, picked up, moved and dispensed in respective dispensing positions by respective single reagent dispensing arms in a similar manner to the sample operation. The chemical reaction is then monitored by photometer means preferably having a plurality of photometric detectors such that radiation passes through each of the cuvettes and the fluids therein during each cycle of the system. Just prior to the sample dispensing position the cuvette

is cleaned and tested to ensure that all the previously added fluids have been removed prior to receiving a new sample. Any one sample may be tested with different reagents or reagent mixtures in different aliquots placed in separate cuvettes at each wavelength as desired. Each sample aliquot and reagent mixture may be measured to determine the rate of the chemical reaction and the equilibrium or end point of the reaction or both, if desired. The array of cuvettes is continuous, because it is replenished at the end of each sequence prior to the addition of the new sample. Relative to the cleaning and testing of the sample cuvettes, column 7, lines 39-54 teach that one of the probes (172) will be coupled to a line (174) and to a source of blanking solution (176). The blanking solution, preferably diluent, will be inserted into the cuvette (18) after the cuvette has been washed so that the photometer means (46) may read the blank liquid to see if the cuvette has been cleaned satisfactorily (no contamination from previous samples). This is accomplished by comparing the reading of the photometer means at the optical wavelength that the cuvette was read prior to initiating the just completed test. If the absorbance of the cuvette is within predetermined limits of the previous blank absorbance value, then the cuvette will be utilized in the next series of tests. If the cuvette fails the test, the analyzer will ignore the cuvette and will not dispense any sample or reagent into that cuvette, at least until it has gone through the wash cycle again. In other words the analyzer stores the previous blank absorbance value and compares it with the current blank absorbance value to determine the difference between the two values. If the difference is within a specified limit, the cuvette will be used again, but if it is outside of the specified limit (differs by more than a certain degree), the cuvette will not be used. Ginsberg includes probe washer or washing stations (58,112,156) that wash and/or clean the pipetting mechanisms used to transfer regents and samples.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the contamination absorbance limit as taught by Kopf-Sill or Ginsberg into the admitted prior art or Sakagami references because of the ability to provide a warning that an analysis result is in error as taught by Kopf-Sill or to prevent and analysis from occurring when the contamination is above a specified limit as taught by Ginsberg. It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the probe washers or washing stations as taught by Ginsberg into the admitted prior art or Sakagami

because of the ability to clean the pipetting mechanisms as taught by Ginsberg and because they are examples of devices that are known in the art as taught by Sakagami.

5. Claims 5, 6-8, 10 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over the admitted state of the art as defined by the Jepsen format of the original claims of the instant application or Sakagami in view of Kopf-Sill or Ginsberg as applied to claims 1-4, 6, 9 and 11 above, and further in view of the admitted state of the art as found on page 2, lines 4-25 and page 4, lines 2-10. The prior art admitted through presentation of the original claims in Jepsen format and the Sakagami reference do not teach that there are situations in which reagents can affect subsequent measurement reactions using different reagents.

On page 2 and 4 applicant is describing the related (prior) art. In the cited lines of page 2, a recognition in the prior art is found that some reagents can cause errors in analysis of samples using other reagents. Page 2 then teaches that in "order to avoid this problem, it has been required for the user to examine beforehand the probability of influence of the contamination and to work out a determination system which can preclude the occurrence of contamination. For instance, a method has been used in which the analysis of item C is interposed between the analyses of item A and item B so that the analysis of item B will not be conducted immediately after the analysis of item A." In the cited lines on page 4 applicant admits that devices capable of collecting data on cross-contamination by the reagents with ease are disclosed in JP-A-5-240867, JP-A-7-270428, etc. In JP-A-5-240867, a system is disclosed which memorizes an analysis request pattern with the order of analysis for checking cross-contamination by the reagent dispenser and cells in a predetermined number of channels, and assigns the channels to the respective items of analysis, allowing anyone to easily obtain data on cross-contamination by the reagents.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the methods of the admitted prior art into the Sakagami or admitted prior art teachings because as noted there is a recognition that cross-contamination of reagents can cause errors in analysis and the admitted prior art has proposed methods to reduce or overcome these recognized problems.

6. Applicant's arguments filed November 10, 2004 have been fully considered but they are not persuasive. First applicant appears to be arguing a particular type of contamination, cross-

contamination involving the transfer of reagent with a pipetting mechanism. While this may be one source of cross contamination, the claims are in no way limited to this specific form of contamination. This can be seen from the new clarity rejection above. Thus these arguments are not commensurate in scope with the claims. For this reason, the prior art rejection is still appropriate for the independent claims and several of the new claims. In addition to this, applicant has glossed over that fact that Ginsberg acts on the change in the measurement which is a change in the state of the instrument (the contamination is sufficient affect a subsequent measurement if the cuvette were to be used in that state).

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (571) 272-1265. The examiner's schedule is variable between the hours of about 6:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

A general phone number for the organization to which this application is assigned is (571) 272-1700. The fax phone number to file official papers for this application or proceeding is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Arlen Soderquist

February 2, 2005
ARLEN SODERQUIST
PRIMARY EXAMINER